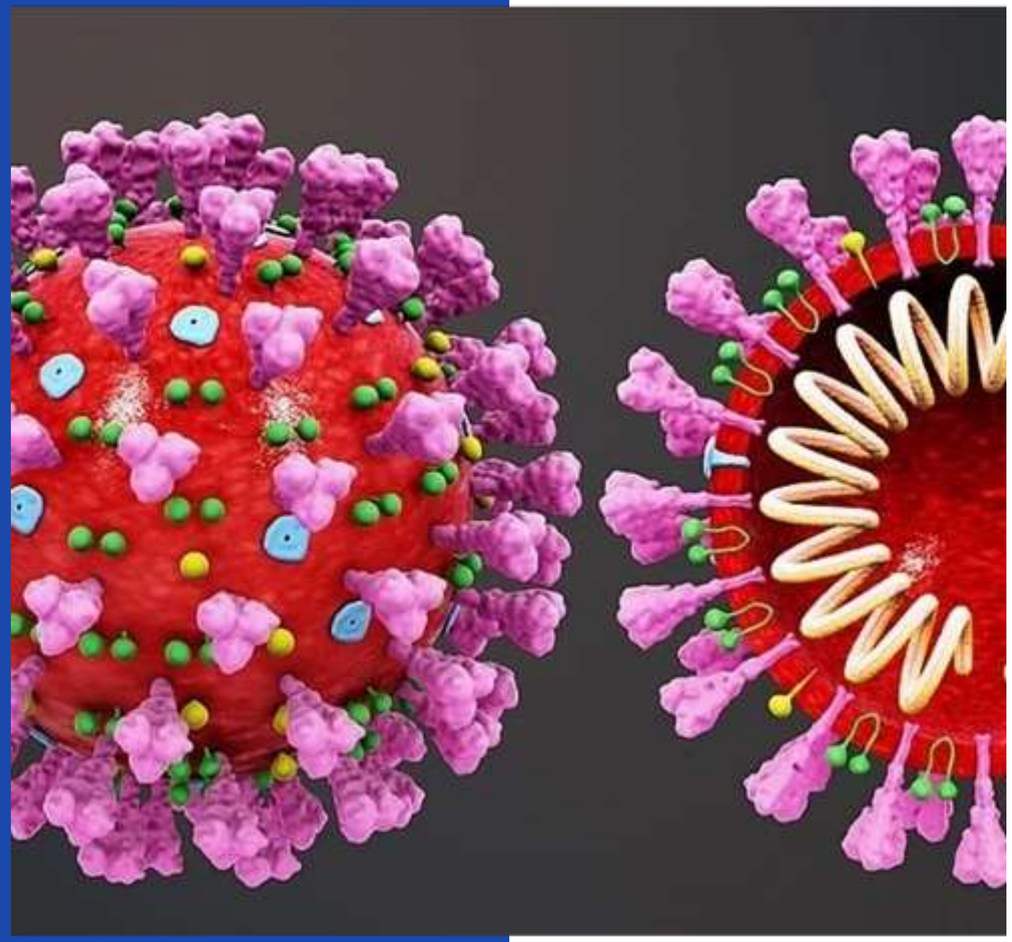

COVID-19
专题科普讲座

2021年2月

厦门燕旭安生物科技有限公司
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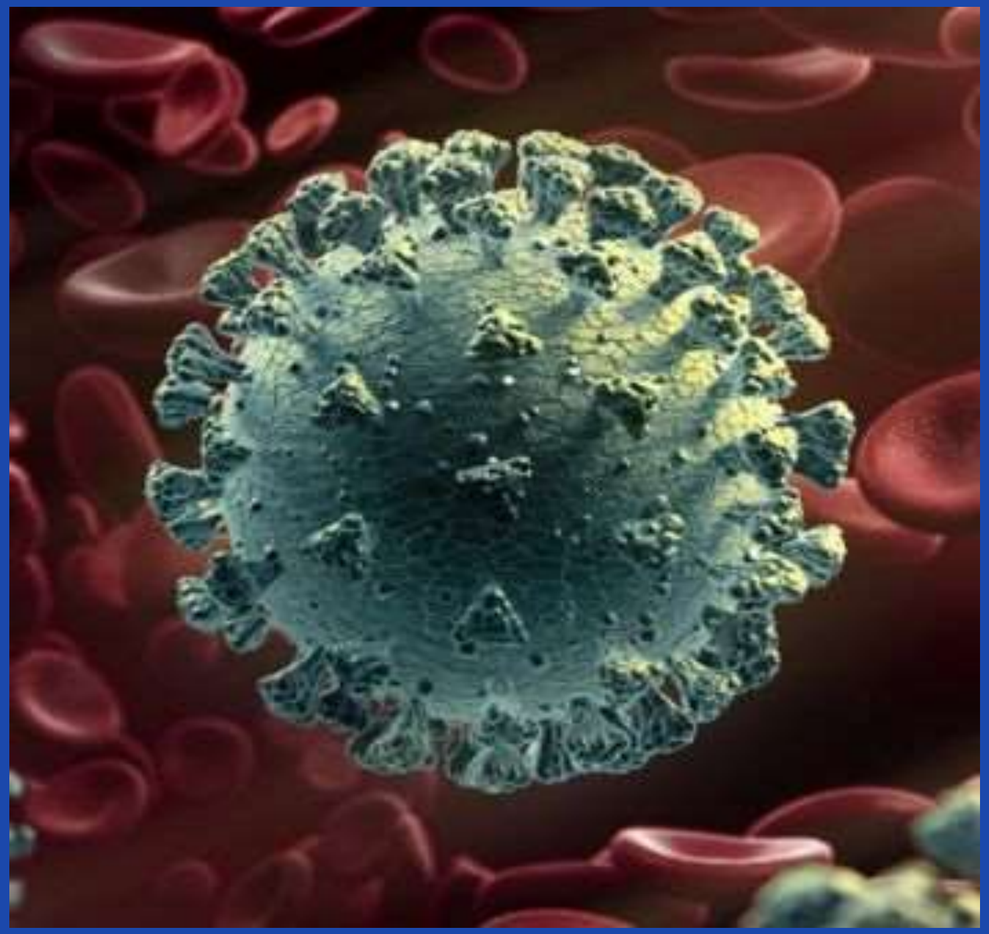
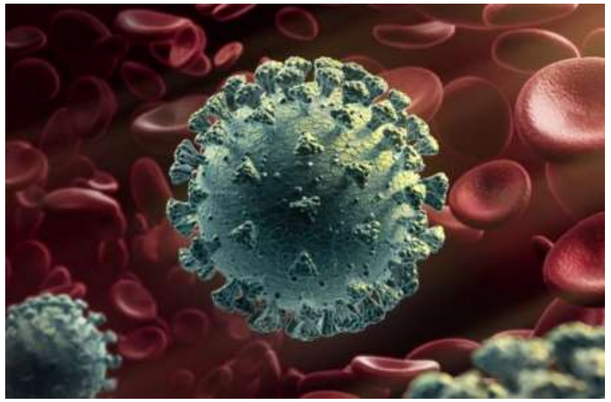
YAN XU AN
BIOTECHNOLOGY

第五部分

病毒变种问题：疫苗是否仍有效



新冠病毒的主要变种

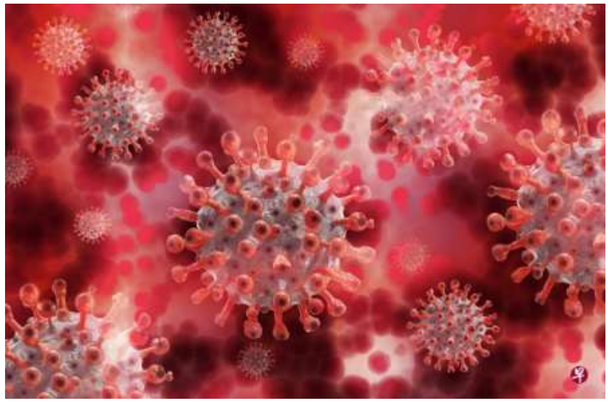


英国变种

即20I/501Y.V1,
VOC202012/01变种,
或称 B.1.1.7变种；含多位点突变，已传播至多个国家，致死风险较高.

南非变种

即20H/501Y.V2 变种，或称B.1.351；与英国变种有部分突变点相同，已传播至多个国家.



巴西变种

即P.1变种，该变种有17 特异突变，包括3个位于S蛋白与受体结合区的突变点.

B.1.1.7 LINEAGE (A.K.A. 20I/501Y.V1 VARIANT OF CONCERN (VOC) 202012/01)

•This variant has a mutation in the **receptor binding domain** (RBD) of the spike protein at position 501, where the amino acid asparagine (N) has been replaced with tyrosine (Y). The shorthand for this mutation is **N501Y**. This variant also has several other mutations, including:

- 69/70 deletion: occurred spontaneously many times and likely leads to a conformational change in the spike protein
- P681H: near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. This mutation has also emerged spontaneously multiple times.

•This variant is estimated to have first emerged in the UK during September 2020.
•Since December 20, 2020, several countries have reported cases of the B.1.1.7 lineage, including the United States.
•This variant is associated with **increased transmissibility** (i.e., more efficient and rapid transmission).
•In January 2021, scientists from UK reported evidence[1] that suggests the B.1.1.7 variant may be associated with an increased risk of death compared with other variants.
•Early reports found **no evidence to suggest that the variant has any impact on the severity of disease or vaccine efficacy.**

B.1.351 LINEAGE (A.K.A. 20H/501Y.V2)

•This variant has multiple mutations in the spike protein, including K417N, E484K, N501Y. Unlike the B.1.1.7 lineage detected in the UK, this variant does not contain the deletion at 69/70.
•This variant was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020, and cases have since been detected outside of South Africa, including the United States
•The variant also was identified in Zambia in late December 2020, at which time it appeared to be the predominant variant in the country.
•Currently there is **no evidence to suggest that this variant has any impact on disease severity.**
•There is **some evidence to indicate that one of the spike protein mutations, E484K, may affect neutralization by some polyclonal and monoclonal antibodies.**

P.1 LINEAGE (A.K.A. 20J/501Y.V3)

•The P.1 variant is a branch off the B.1.1.28 lineage that was first reported by the National Institute of Infectious Diseases (NIID) in Japan in four travelers from Brazil, sampled during routine screening at Haneda airport outside Tokyo.
•The P.1 lineage contains three mutations in the spike protein receptor binding domain: K417T, E484K, and N501Y.
•There is evidence to suggest that some of the mutations in the P.1 variant may affect its transmissibility and antigenic profile, which may affect the ability of antibodies generated through a previous natural infection or through vaccination to recognize and neutralize the virus.

- A recent study reported on a cluster of cases in Manaus, the largest city in the Amazon region, in which the P.1 variant was identified in 42% of the specimens sequenced from late December.[5] In this region, it is estimated that approximately 75% of the population had been infected with SARS-CoV2 as of October 2020. However, since mid-December the region has observed a surge in cases. The emergence of this variant raises concerns of a potential increase in transmissibility or propensity for SARS-CoV-2 re-infection of individuals.

•This variant was identified in the United States at the end of January 2021.

抗体药可能对新变种效力减弱—突变逃逸

REPORT

Prospective mapping of viral mutations that escape antibodies used to treat COVID-19

Tyler N. Starr[1,*], Allison J. Greaney[1,2,3,*], Amin Addetia[1,4], William W. Hannon[1,4], Manish C. Choudhary[5], Adam S. Din…
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CORONAVIRUS

Prospective mapping of viral mutations that escape antibodies used to treat COVID-19

Tyler N. Starr[1]*, Allison J. Greaney[1,2,3]*, Amin Addetia[1,4], William W. Hannon[1,4], Manish C. Choudhary[5], Adam S. Dingens[1], Jonathan Z. Li[5], Jesse D. Bloom[1,2,6]†

Antibodies are a potential therapy for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but the risk of the virus evolving to escape them remains unclear. Here we map how all mutations to the receptor binding domain (RBD) of SARS-CoV-2 affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016. These complete maps uncover a single amino acid mutation that fully escapes the REGN-COV2 cocktail, which consists of two antibodies, REGN10933 and REGN10987, targeting distinct structural epitopes. The maps also identify viral mutations that are selected in a persistently infected patient treated with REGN-COV2 and during in vitro viral escape selections. Finally, the maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains. These complete escape maps enable interpretation of the consequences of mutations observed during viral surveillance.

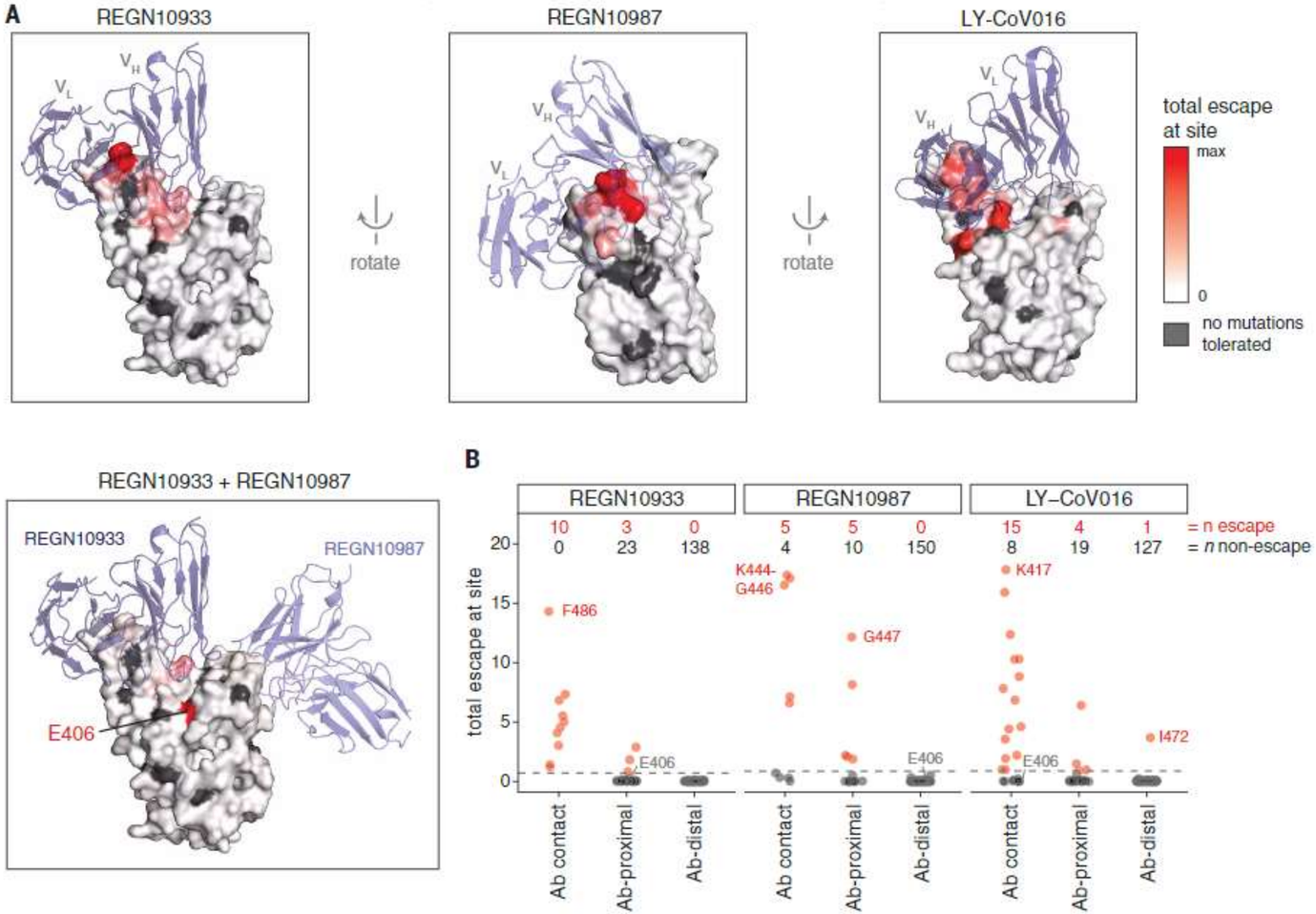

Fig. 4. Structural context of escape mutations. (**A**) Escape maps projected on antibody-bound RBD structures. [REGN10933 and REGN10987: Protein Data Bank (PDB) ID 6XDG (*11*); LY-CoV016: PDB ID 7C01 (*13*)]. Antibody heavy- and light-chain variable domains are shown as blue cartoons, and the RBD surface is colored to indicate how strongly mutations at that site mediate escape (white indicates no escape, red indicates strongest escape site for that antibody or cocktail). Sites where no mutations are functionally tolerated are colored gray. (**B**) For each antibody, sites were classified as direct antibody contacts (non-hydrogen atoms within 4 Å of antibody), antibody-proximal (4 to 8 Å), or antibody-distal (>8 Å). Each point indicates a site, classified as escape (red) or non-escape (black). The dashed gray line indicates the cutoff used to classify sites as escape or non-escape (see materials and methods for details). Red and black numbers indicate how many sites in each category are escape or non-escape sites, respectively. Interactive visualizations are at https://jbloomlab.github.io/SARS-CoV-2-RBD_MAP_clinical_Abs/, and hypothesized mechanisms of escape and additional structural details for labeled points are shown in fig. S6.

病毒变种对疫苗有效性的影响

以往经验：

- 无需更改疫苗：麻疹measles
- 不断更改疫苗：流感influenza

疫苗对新冠病毒变种的有效性

新冠疫苗是整个S蛋白、或者整个病毒颗粒灭活后制备而成，因此一般对变种（个别氨基酸变化）还会有保护力，但由于三维结构等因素的变化，可能保护力会有所减弱。

变种的主要问题：感染力/传播率，致死风险